Modulation of multidrug resistance by immunosuppressive agents: cyclosporin analogues, FK506 and mizoribine.

Abstract	It has recently been reported that an immunosuppressive agent, cyclosporin A, shows a potent overcoming effect on multidrug resistance (MDR). We studied the presence of such a modulating effect of cyclosporin analogues and other immunosuppressive agents, FK506 and mizoribine, in human multidrug-resistant ovarian cancer cells (TAOV/A0.2). The intensity of the overcoming effect of cyclosporin analogues against adriamycin resistance was found to be in the other of cyclosporin D greater than A greater than C greater than H. It was found that cyclosporin D, which has relatively weak immunosuppressive activity, overcame adriamycin resistance in the multidrug-resistant ovarian cancer cells to a remarkable degree. On the other hand, it was found that FK506, a new potent immunosuppressant, could also distinctly modulate adriamycin-resistance. It was found that FK506 conferred chemosensitization upon adriamycin with reincreasing intracellular adriamycin accumulation in MDR cells which was far less than the parent strain. However, in the case of mizoribine, no modulation of drug resistance existed. Such modulation was not necessarily accompanied by immunosuppressive activity and the two functions were thought to be based on different mechanisms.
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